the application is requested in view of the following amendments and remarks.

Remarks

Claims 25-27, 43-45 and 55-57 were rejected based solely on 35 U.S.C. §102(b), as anticipated by Heldin et al., *Nature* (1986) 319:511-514 ("Heldin"). The Action states that the Declaration of Christer Betsholtz, Ph.D., submitted with the previous response, is insufficient to overcome the rejection. The Action asserts:

> The prior art teaching of Heldin et al. clearly demonstrates a single band on a silver-stained gel which is recognized in the prior art as being indicative of a homogeneous preparation as is the amino acid sequencing which did not detect any other proteins present.

Office Action, pages 4-5, bridging paragraph. However, applicants continue to assert that the present claims patentably distinguish over Heldin.

Applicants reiterate that all of the pending claims relate to PDGF A-chain homodimer preparations produced recombinantly in nonhuman cells. The preparations are free of human protein contaminants since the only human structural gene present in the recombinant plasmids is the gene encoding human PDGF. Such purity cannot be achieved absent the gene encoding PDGF. Heldin does not describe the gene or recombinant methods for producing PDGF A-chain.

Rather, Heldin isolates a growth factor from human

osteosarcoma cells using conventional protein chemistry techniques. Such techniques must result in a protein preparation that includes at least trace amounts of other human protein contaminants since 100% purity is never achievable. As confirmed in paragraph 5 of Dr. Betsholtz's Declaration submitted previously, the product of each of the chromatographic columns used by Heldin to purify ODGF "would inherently include at least small amounts of human proteins other than human ODGF since the ODGF was isolated from human osteosarcoma cells." Moreover, Dr. Betsholtz has stated that the purification methods used by Heldin "cannot result in a protein product free of contaminating protein." Dr. Betsholtz further notes in paragraph 5 of the Declaration "it is a virtual certainty that trace amounts of human proteins were present in the ODGF preparations that were not detected..."

The Action disputes these statements and argues that no bands other than PDGF A-chain homodimer were visible in silver-stained SDS polyacrylamide gels and no other amino acid sequence was obtained from the PDGF A-chain homodimer preparation. However, it is well known that although silver-staining is sensitive, there are thresholds below which proteins are undetectable. Thus, the absence of other bands is not necessarily indicative of homogeneity.

Applicants submit that the Examiner has improperly dismissed Dr. Betsholtz's Declaration which is considered by applicants to be highly probative regarding patentability of the present claims. Dr. Betsholtz is a skilled artisan in

the subject field and a coauthor on the Heldin publication which forms the basis of the present rejection! By dismissing the Declaration, it appears the Examiner has substituted his own knowledge with respect to the cited art for that of Dr. Betsholtz's. Applicants respectfully request that if the Examiner maintains the assertion that the Declaration is inadequate to overcome the instant rejection, he present his qualifications as one of skill in the art, as well as facts evidencing that the purification techniques used by Heldin can result in a protein preparation lacking all human protein contaminants, for the record in an affidavit pursuant to 37 CFR §1.107(a).

Hence, applicants maintain their position that a purified protein from a human cellular source will necessarily contain human protein contaminants. Conventional protein purification methods simply cannot result in a completely pure product but, rather one which would inherently include at least small, perhaps undetectable by then available techniques, amounts of human proteins other than human PDGF.

Additionally, it is axiomatic that "[i]nherency ... may not be established by probabilities or possibilities.... The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *In re Oelrich*, 212 U.S.P.Q. 323, 326 (CCPA 1981) (quoting *Hansgirg v. Kemner*, 40 U.S.P.Q. 665, 667 (CCPA 1939)).

Finally, the Action states that newly submitted claims 55-57, directed to preparations for topical administration, are also anticipated by Heldin based on the disclosure of phosphate buffer in the legend of Figure 1. However, as explained above, the preparation described in Figure 1 is not believed to be completely devoid of other human proteins. Furthermore, the disclosure of phosphate buffer is with reference to subparts (a) and (b) of Figure 1. Figures 1(a) and 1(b) clearly relate to heterogeneous mixtures of proteins, as evident from the multiple bands present in the figures. Accordingly, the legend of Figure 1 does not render claims 55-57 anticipated, as argued by the Office.

Conclusion

Applicants respectfully submit that the claims define an invention which is novel and nonobvious over the art. Accordingly, allowance is believed to be in order and an early notification to that effect would be appreciated.

Please direct all further communications in this application to:

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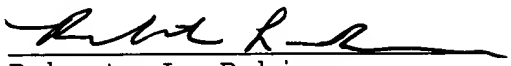
Respectfully submitted,

By: 

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